REMARKS

Claims 1-43 and 49-50 stand cancelled and claims 53-57 have been added. No new matter has been added by virtue of these amendments; support therefor can be found throughout the specification (see, for instance, pages 20-23) and in the original claims of the application.

Consideration and entry of the proposed amendments is earnestly solicited at this time.

Claims 43-48, 51 and 52 stand rejected under USC 35 §112, on the grounds of enablement. The position is taken that the specification does not describe a protocol for prophylactic treatment of a disease related to phosphodiesterase isoenzyme.

The rejection is respectfully traversed. The Office Action expressly acknowledges that a disease related to a phosphodiesterase isoenzyme is usually a chronic disease. Such diseases include, for example, asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), and cystic fibrosis. As is often the case, individuals who suffer from these chronic diseases experience asymptomatic periods. Thus, although the individual may not be suffering an 'outbreak', e.g., exhibiting symptoms of the disease at any given time, the individual nonetheless remains susceptible to and at risk for repeated occurrences of the disease. Methods of the invention would be suitable for administration to such individuals in a prophylactic manner in order to avoid repeated outbreaks and mitigate the chronic effects of the diseases.

Moreover, the specification provides ample support for prophylactic methods of treatment. In Example A, for instance, the experimental protocol teaches the addition of compounds of the present invention to the guinea-pig isolated trachea organ bath and the system was allowed to equilibrate before commencement of

electrical stimulation. Results of these experiments as shown in Figures 2 - 8, clearly demonstrate when compared with control, the compounds of the present invention (such as the compounds of Examples 1, 8, 9, 10, 11, and 13) caused complete inhibition (prophylactic treatment) of the contractile response to electrical field stimulation. Indeed, the effect was maintained for more than 2 – 4 hours.

Moreover, in Example E the experimental protocol of *in vivo* test 1 teaches testing in a model of histamine induced bronchospasm wherein conscious guinea-pigs were first exposed to dry powder of the compounds of the present invention or control at various concentrations. At various times after exposure to the drug the animals were anaesthetized and challenged with varying doses of histamine. Total airway resistance and mean arterial blood pressure were recorded. Results showed compounds of the present invention (such as the compound of Example 1) when administered as dry powder provided significant protection (prevention) against histamine induced bronchospasm over a 5.5 hour period and clearly demonstrated the preventive/prophylactic use of these compounds.

Further, in Example E the experimental protocol of *in vivo* test 3 teaches testing in a model of antigen induced eosinophilia in the ovalbumin sensitized guinea-pig. Results showed compounds of the present invention (such as the compound of Example 1) when administered orally 1 hour prior to antigen challenge, significantly inhibited (prevented) the recruitment of eosinophils to the lungs following antigen challenge in sensitized guinea pigs. Similarly, exposure to dry powder of compounds of the present invention (such as the compound of Example 1) 1.5 hours prior to antigen challenge, significantly inhibited (prevented) the recruitment of eosinophils to the lungs.

In view of the foregoing, it is respectfully submitted that the enablement rejection be withdrawn.

In view of the within remarks and amendments, Applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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